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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,683	03/20/2000	MICHAEL ANTHONY CAWTHORNE	00537/163002	7045

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BRIAN R MORRILL
BIOMEASURE INC
27 MAPLE STREET
MILFORD, MA 01757-3650

EXAMINER
MOHAMED, ABDEL A

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/423,683	CAWTHORNE ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,8,18 and 32-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,8,18 and 32-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

CONTINUED EXAMINATIONUNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/24/02 and 2/19/03 have been entered.

ACKNOWLEDGMENT OF PRIORITY, PRELIMINARY AMENDMENT, REMARKS, IDS, STATUS OF THE APPLICATION AND CLAIMS

2. This application is filed under 35 U.S.C. 371 on 3/20/00 having a filing date of 5/13/98 of PCT/EP98/02998, which is a Continuation of U.S. Patent Application No. 08/855,311, with a filing date 5/13/97, now abandoned. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The preliminary amendment, Information Disclosure Statement (IS) and Form PTO-1449 filed 2/19/03 and 6/24/02, respectively are acknowledged, entered and considered. In view of Applicant's request claims 1 and 6 have been amended, claims 2-5, 7, 9-17and 19-30 have been canceled and claims 32-55 have been added. Thus, claims 1, 6, 8, 18 and 32-55 are now pending in the application. The objections to the specification, abstract and claims, and the rejection under 35 U.S.C. 101 and partial rejection under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicant's amendment, remarks and cancellation of claims filed 2/19/03. However, the partial

rejection under 35 U.S.C. 112, second paragraph and the rejections under 35 U.S.C. 102(b) and 103(a) over the prior art of record are maintained.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

It is noted that Applicant has canceled most of the claims rejected under U.S.C. 112, second paragraph and amended claims 1 and 6 to be consistent with originally filed claims 1 and 6. Applicant has not argued the rejection under 35 U.S.C. 112, second paragraph with respect to claims 6 and dependent claims thereof (i.e., claims 8 and 18), and canceled claims 23-26 (i.e., now newly presented as claims 37, 43, 49 and 55, respectively). Thus, the previous rejection with respect to the above claims is maintained as reiterated below: Claims 6, 8, 18 and newly submitted claims 37, 43, 49 and 55 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recite the limitations "of lowering the amount of triacylglycerols, glycerol, or cholesterol in the blood of a patient in need of such lowering" in lines 1-2. There are insufficient antecedent basis for these limitations in claim 1 or claim 6.

Newly submitted claims 37, 43, 49 and 55 (canceled claims 23-26) are indefinite and confusing in the recitation "Tyr(I)" because the expression is not defined in the specification or in the claim. Appropriate clarification is required.

CLAIMS REJECTION-35 U.S.C. § 102(b)

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 8, 18 and newly submitted claims 32-33, 38-39, 44-45 and 50-51 remain rejected under 35 U.S.C. 102(b) as being anticipated by Moller et al. (Clin. Science, Vol.75, pp. 345-350, 1988).

Moller et al. disclose the use of mixed SSTR-2/SSTR-5 agonist (e.g., SMS 201-995 or somatostatin-14) for the method of treating hyperlipidemia in which the reference clearly demonstrates the lowering of triglyceride levels (See e.g., page 348, Fig. 5) and blood glycerol levels (See e.g., Fig. 4) as directed to claims 1, 6, 8 and 18 . Also, the reference discloses a pharmaceutical composition for treatment of hyperlipidemia or lowering triacyglycerols or glycerols or cholesterol in the blood of a patient comprising an effective amount of a somatostatin type-5 receptor agonist (SSTR-5 agonist) as directed to newly submitted claims 32-33, 38-39, 44-45 and 50-51 (See e.g., page 345 and 347). Thus, the reference clearly anticipates the method of treating hyperlipidemia by administering a therapeutically effective amount of a type-5 selective somatostatin agonist (SSTR-5 agonist) to a patient to reduce triglyceride , glycerol and cholesterol levels in the blood of said patient and to a pharmaceutical formulations thereof as claimed in claims 1, 6, 8, 18, 32-33, 38-39, 44-45 and 50-51.

CLAIMS REJECTION-35 U.S.C. § 103(a)

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

It is noted that Applicant has canceled method claims 2-5, 7, 9-17 and 19-26 as well as composition claims 27-28 and added claims 32-55 as composition claims based on the subject matter of former claims 27-28. Since composition claims 27-28 along currently pending method claims 1, 6, 8 and 18 have been rejected previously under 35 U.S.C. 103(a) as reiterated below:

Claims 1, 6, 8, 18 and 32-55 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. (Clin. Science, Vol. 75, pp. 345-350, 1988) taken with WO 96/35950 or Degrado (attachment provided in the previous Office action, Paper No. 14).

The primary reference of Moller et al., disclose the use of mixed SSTR-2/SSTR-5 agonist (e.g., SMS 201-995 or somatostatin-14) for the method of treating hyperlipidemia in which the reference clearly demonstrates the lowering of triglyceride levels (See e.g., page 348, Fig. 5) and blood glycerol levels (See e.g., Fig. 4) as directed to claims 1, 6, 8 and 18 . Also, the reference discloses a pharmaceutical composition for treatment of hyperlipidemia or lowering triacyglycerols or glycerols or cholesterol in the blood of a patient comprising an effective amount of a somatostatin type-5 receptor agonist (SSTR-5 agonist) as directed to newly submitted claims 32-33, 38-39, 44-45 and 50-51 (See e.g., page 345 and 347). The primary reference differs from claims 1, 6, 8, 18 and 32-55 in not teaching the use of highly selective SSTR-5 agonists (e.g., ratio SSTR-2/SSTR-5>2) and the modification of the peptide to include D-Phe and D-Trp. However, the reference of WO 96/35950 on page 17 Table II, discloses that the compound has a K of 7.0 nM for SSTR-5 receptor (ratio SSTR-2/SSTR-5 = 0.07). Thus, the prior art discloses several somatostatin analogues with the ratios as shown on Table II), hence, it appears to be obvious to one of ordinary skill in the art to test whether these or related compounds have any pharmaceutical effect on blood lipid levels.

Further, WO 96/35950 discloses Applicant's method using Applicant's claimed peptide Phe-Phe-Phe-Trp-Lys-Thr-Phe-Thr-NH_2 , However, the reference does not teach modification of peptide to include D-Phe and D-Trp; but, this known modification of the peptide of WO 96/35590 would have been obvious to one of ordinary skill in the art because Degrado discloses that introduction of D-amino acids into a peptide is "a popular modification" that results in analogs with enhanced stabilities to enzymatic degradation. Thus, the combined teachings of the prior art make obvious the claimed

invention, absent of sufficient objective factual evidence e or unexpected results to the contrary.

ARGUMENTS ARE NOT PERSUASIVE

6. **CLAIMS REJECTION-35 U.S.C. § 102(b)**

The rejection of claims 1, 6, 8, 18 and newly submitted claims 32-33, 38-39, 44-45 and 50-51 under 35 U.S.C. 102(b) as being anticipated by Moller et al. (Clin. Science, Vol. 75, pp. 345-350, 1988).

Applicant's arguments filed 2/19/03 have been fully considered but they are not persuasive. Applicant has argued that the SMS-201-995 does not fall within Applicant's definition of an SSTR-5 agonist as set forth in the application, because the SSTR-5 are not below 5 nM. Therefore, Moller does not disclose the claim element of administering a therapeutically effective amount of an SSTR-5 agonist is unpersuasive. Contrary to Applicant's arguments, the specific limitation of Ki value of less than 2 nM is not recited in the rejected claims. Nevertheless, the claims are interpreted in light of the specification, limitation from specification or unrejected claim(s) are read into the rejected claims. See *In re Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, Applicant's arguments are not commensurate to the scope of the rejected claims. Further, the term "comprising" would not exclude other somatostatins. Thus, the Moller et al., reference clearly discloses the method of treating hyperlipidemia by administering a therapeutically effective amount of a type-5 selective somatostatin agonist (SSTR-5 agonist) to a patient to reduce triglyceride, glycerol and cholesterol levels in the blood of

said patient and to a pharmaceutical formulations thereof as claimed in claims 1, 6, 8, 18, 32-33, 38-39, 44-45 and 50-51.

Applicant asserts that the prior art of Moller does not anticipate claims 1 and 6 because the claims are directed to "a method of treating hyperlipidemia in a patient in need of such treatment" (claim 1) or "a method of lowering acyglycerols, glycerol or cholesterol in a patient in need of such lowering" (claim 6); and concludes by stating "Whether these finding would be reproduced in patients treated chronically with the drug is unknown" is noted. However, contrary to Applicant's assertion, under Discussion, the reference of Moller clearly states that the effect of somatostatin and its analogues on gastrointestinal tract have suggested from **clinical application** of these compounds in disease state (i.e., in need of such treatment) such as severe diarrhea, diabetes mellitus and certain endocrine neoplasia. Although, the experiment was conducted on healthy individuals, however, the reference concludes by stating we have found the 50 ug of SMS 201-995 given preprandially delays gastrointestinal transit time, lowers postprandial and basal levels of triglyceride and delays monosaccharide absorption in normal man. Whether these findings would be reproduced in patients treated chronically with the drug is unknown. The above statement is an invitation for one skilled in the art to try the protocol in disease state (i.e., in need of such treatment) and it is expected that the method/protocol would work unless Applicant demonstrates otherwise because substantially the same composition for the same purpose is used.

Further, with respect to composition claims 32-33, 38-39, 44-45 and 50-51, although, the reference discloses a pharmaceutical composition for treatment of

hyperlipidemia or lowering triacyglycerols or glycerols or cholesterol in the blood of a patient comprising an effective amount of a somatostatin type-5 receptor agonist (SSTR-5 agonist); however, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re Spada,* 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969).

CLAIMS REJECTION-35 U.S.C. § 103(a)

7. The rejection of claims 1, 6, 8, 18 and 32-55 under 35 U.S.C. 103(a) as being unpatentable over Moller et al. (Clin. Science, Vol. 75, pp. 345-350, 1988) taken with WO 96/35950 or Degrado (attachment provided in the previous Office action, Paper No. 14).

Applicant has argued that none of the cited references either singularly or in combination teach or suggest Applicant's claimed invention, in particular, none of the

cited reference teaches the use of a compound with a Ki of less than 5 nM for the somatostatin type-5 receptor to treat hyperlipidemia with a patient population specifically in need of treatment for such disorder is unpersuasive. Contrary to Applicant's arguments, the secondary reference of WO 96/35950 clearly on page 17 Table II, discloses that the compound has a K of 7.0 nM for SSTR-5 receptor (ratio SSTR-2/SSTR-5 = 0.07). Also, on page 17, lines 9-11, the reference states that the Ki values (in nM) for the test somatostatin analogs are listed in Table II (where LC is 0.05 nM and LEC is 0.18 nM). Thus, the prior art discloses several somatostatin analogues with the ratios as shown on Table II), hence, it appears to be obvious to one of ordinary skill in the art to test whether these or related compounds have any pharmaceutical effect on blood lipid levels.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at the time the invention was made to employ a method of treating hyperlipidemia by administering a therapeutically effective amount of mixed SSTR-2/SSTR-5 agonist to a patient to reduce triglyiceride and glycerol levels in the blood of said patient and to a pharmaceutical formulation thereof. Thus, it is made obvious by the combined teachings of the prior art since the instant invention's methods of using of a compound with a Ki less than 5 nM for the somatostatin type-5 to treat hyperlipidemia within a patient population specifically in need of treatment of such disorder; which fall within the scope of the prior art method and composition would have been obvious because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselet*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Betz*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the

references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

The following is a new ground of rejection:

HEADING FOR NONSTATUTORY DOUBLE PATENTING

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

REJECTION OF OBVIOUSNESS-TYPE DOUBLE PATENTING

9. Claims 1, 6, 8, 18 and 32-55 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,004,928. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed invention (Serial No. 09/423,683) as claimed in claims 1, 6, 8 and 18 is directed to a method of treating hyperlipidemia by administering a therapeutically effective amount of a type-5 selective somatostatin agonist (SSTR-5 agonist) to a patient to reduce triglyceride , glycerol and cholesterol levels in the blood of said patient as claimed in claims 1-23 of '928 patent. Although, claims 1-23 of '928 patent use specific compositions which are not recited in method claims of claim 1, 6, 8 and 18 in the instant application; however, the specific compositions claimed in claims 32-55 is the same compositions used in method claims 1-23 of '928 patent. Thus, from the claims, it is an obvious variation to select or use either the composition claims or method claims separately or in combination because in both situations (i.e., the compositions claimed in claims 32-55 are used in the method of claims 1-23 of '928 patent) the same compositions are used for the same purpose. Therefore, both inventions are an obvious variation of the other since the instantly claimed invention claims methods of treatment as claimed in claims 1, 6, 8, and 18 as well as compositions claims of claims 32-55 which are claimed in method of treatment claims of 1-23 of '928 paten for the same purpose, and as such, one of ordinary skill in the art would envision both sets of claims as one invention and obvious variation of each other.

CONCLUSION AND FUTURE CORRESPONDENCE

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

Mohamed/AAM

July 28/2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600